Remarks

Claims 1, 11, 12, 14-23, 29, 37-40, 50-53, 59, 60, 84, 94-99, 114-116, 121-126, 133-144 and 151-163 are presently pending in the subject application.

Reconsideration and allowance are respectfully requested in view of the above amendments and the following remarks.

Claims 87-93, 100-113, 117-120, 127-132 and 145-150 are canceled herein without prejudice to the prosecution of the subject matter of these claims in this or a future continuing application.

Claims 1, 21-23, 29, 38-40, 53, 59, 60, 84, 94-99, 114-116, 121-126, 133-144 and 151-159 have been amended herein. These amendments to the claims do not introduce new matter.

Claims 1, 53 and 84 have been amended to recite a hybridization assay probe or oligonucleotide containing a target binding region that fully hybridizes to a target sequence present in nucleic acid derived from a *Cryptosporidium parvum* organism. The "fully hybridizes" language is supported in the specification *passim* (*see, e.g.*, paragraph bridging pages 17 and 18). With the Examiner's permission during a telephonic interview with Applicant's representative on the below indicated date, claims 1, 53 and 84 have been further amended to recite a target sequence selected from the Markush grouping of SEQ ID Nos. 5, 9, 13 and 17 in place of the former Markush grouping of SEQ ID Nos. 6, 10, 14 and 18. The base sequences of SEQ ID Nos. 5, 9, 13 and 17 fully contain the base sequences of previously elected SEQ ID Nos. 6, 10, 14 and 18. Applicants wish to thank the Examiner for permitting them to make this change to the claims. It is noted for the record that no other substantive issues were discussed during this interview.

Claims 23, 29, 38-40, 53, 59, 60, 84, 94, 95, 114-116 and 155 have been amended to specify that the claimed oligonucleotide or target binding region is at least 18 bases in length and fully hybridizes to the recited target sequence for that oligonucleotide or target binding region. The length limitation of these amended claims is supported in the specification at, for example, page 4, lines 22-26 (probes), the sentence bridging pages 5 and 6 (helper oligonucleotides), and page 31,

lines 7-9 (amplification oligonucleotides). And, as indicated above, the "fully hybridizes" language is supported in the specification *passim* (*see, e.g.*, paragraph bridging pages 17 and 18).

Claims 21, 22, 96-99, 121-126, 134, 136, 138, 140, 142, 144, 152, 154, 157 and 159 have been amended to indicate that the base sequence of the recited oligonucleotide or target binding region of the probe or oligonucleotide is perfectly complementary to the corresponding target sequence. Support for this amendment can be found in the specification at, for example, page 4, lines 22-26, page 5, lines 26-27, page 6, lines 22-23, page 17, lines 21-25, and page 51, lines 1-2.

Claims 114-116 have been amended to require that the base sequences of the target binding regions of the amplification oligonucleotides of these claims are at least 80% complementary to the base sequences of the corresponding target sequences. The amended language of these claims originally appeared in claims 121-123.

Claims 160-163 are new and depend from claims 1, 37, 53 and 84, respectively. Each of these claims recites a probe or oligonucleotide have a target binding region that is at least 18 bases in length. This amendment is supported in the specification at, for example, page 4, lines 22-26.

Objection to the Specification

The disclosure is objected to by the Examiner for containing an embedded hyperlink. The Examiner has requested that Applicants remove the browse executable code. To that end, Applicants have amended the specification herein to render the disclosed hyperlink inactive. Accordingly, withdrawal of this objection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1, 14, 19-23, 29, 37-40, 50-53, 59, 60, 84, 93-99, 106, 107, 114-126, 133-144 and 150-159 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Zhu *et al.* (*J. Infectious Disease*, 177:1443-1446 (1998)) in view of Williams *et al.* (U.S. Patent No. 6,146,855) and Xiao *et al.* (*Appl. Environ. Microbiol.*, 65(8):3386-3391 (1999)) in view of Hogan

et al. (U.S. Patent No. 5,595,874). Applicants respectfully traverse this rejection for the reasons that follow.

The Examiner relies upon Zhu for teaching a method of detecting *Cryptosporidium* using genus-specific primers from the 18S rRNA. While conceding that Zhu does not teach using SEQ ID NO:6 as the target sequence for the probes and primers, the Examiner points out that Williams provides a sequence alignment between *C. parvum*, *C. muris* and *C. baileyi* and that the sequences of SEQ ID Nos. 6, 29 and 48 are embedded within the sequence alignment. Xiao is cited for disclosing a comparison study of various *Cryptosporidium* isolates and for providing GenBank accession numbers for nucleotide sequences that were compared. Xioa is also cited for teaching an alignment of the sequences for identifying differences between the isolates. Finally, Hogan is cited by the Examiner for teaching a method of comparing rRNA variable region sequences to design probes for distinguishing between organisms. From these disclosures, the Examiner concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the genus-specific primers of Zhu using the alignments provided by Williams and Xiao and the guidance taught by Hogan to obtain the invention as a whole.

In support of the Examiner's argument that the invention as a whole would have been *prima facie* obvious, the Examiner relies us the Court's holding in *In re Deuel*, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). Specifically, the Examiner quotes a portion of the Court's decision which provides that a *prima* facie case of obviousness is normally based upon structural similarity between a prior art compound and the claimed compound. From this the Examiner argues that the claimed primers simply represent functional equivalents of the probes and primers of Zhu. But whether the claimed compounds perform the same function is not the standard established by the Court in *In re Deuel*, as evidenced by the section quoted by the Examiner, and cannot be relied upon for establishing a *prima facie* case of obviousness. Based on this improper functional equivalence argument, the

Examiner goes on to contend that skilled artisans would have been motivated to find alternate compounds with improved properties. However, as Zhu states that primers CF201 and CR201 were specific to the genus *Cryptosporidium* (*see* Zhu at page 1444, col. 2), the requisite motivation to search for new primers and probes appears to be missing, absent a specific showing by the Examiner.

Applicants further submit that the combination of references relied upon by the Examiner teaches away from rather than renders obvious the claimed invention. As the Examiner has noted in Applicant's companion application, U.S. application Serial No. 09/954,695 ("the '695 application"), skilled artisans will generally select regions for probing that have the greatest variability in order to design probes having the greatest specificity for their intended target. *See* Final Action in the '695 application at page 4, lines 20-22, and page 5, line 7 *et seq.* With this motivation in mind, Applicants note that Williams discloses and specifically identifies regions of variability in the 18S rRNA gene sequences of *C. parvum*, *C. muris* and *C. baileyi* in Figures 3A-C having greater variability than the region targeted by the claimed probes. *See* Williams at col. 2, lines 10-23 (regions identified as 'c', 'd', 'e' and 'f' in Figures 3A-C. Consequently, Applicants submit that it is those regions of variability specifically identified by Williams that would have been suggested to skilled artisans at the time of the claimed invention for designing probes specific for *C. parvum* rather than the region targeted by Applicants' claimed probes. Thus, Applicants submit that one skilled in the art at the time of the claimed invention, in possession of the combination of references cited by the Examiner and seeking the greatest degree of probe specificity for detecting *C. parvum* organisms, as argued by the Examiner, would have been led away from the claimed probing region.

Claims 11-13 and 15-18 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Zhu *et al.* (*J. Infectious Disease*, 177:1443-1446 (1998)) in view of Williams *et al.* (U.S. Patent No. 6,146,855) and Xiao *et al.* (*Appl. Environ. Microbiol.*, 65(8):3386-3391 (1999)) in view of Hogan *et al.* (U.S. Patent No. 5,595,874) as applied to claims 1, 6-10, 14,

19-23, 29, 37-40, 50-53, 59, 60, 84, 93-99, 106, 107, 114-126, 133-144 and 150-159 above, and further in view of Becker *et al.* (U.S. Patent No. 6,361,945). Applicants submit that the teachings of Becker do not overcome the deficiencies noted above in the teachings of Zhu, Williams and Xiao when combined with the teachings of Hogan.

For the reasons set forth above, Applicants submit that the presently pending claims are fully patentable in view of the cited references, considered separately or in any combination. Accordingly, withdrawal of the Examiner's Section 103(a) rejections is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1, 11-21, 23, 29, 37-40, 50-53, 59, 60, 84, 94-97, 114-116, 121-125, 133, 135, 137, 139, 141, 143, 151, 153, 155, 156 and 158 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as lacking written description support. Applicants submit that the Examiner's stated basis for this rejection is overcome by the amendments to the claims herein. Specifically, the claims now minimally require that an oligonucleotide, or the target binding region of a probe or oligonucleotide useful as a detection probe, be of sufficient length to fully hybridize to the recited target sequence with specificity under stringent conditions (*i.e.*, the recited probe or oligonucloetide does not hybridize to nucleic acid derived from a *C. muris*, *C. baileyi* or *C. wrairi* organism to form a probe:non-target or oligonucleotide:non-target hybrid stable for detection under stringent conditions). Other claims include more restrictive length limitations, further requiring that an oligonucleotide, or the target binding region of a probe or oligonucleotide, be at least 18 bases in length and fully hybridize to the recited target sequence under stringent or amplification conditions. As indicated above in the introductory remarks, an 18 base length minimum for an oligonucleotide or target binding region of a probe or oligonucleotide is supported in the specification at, for example, page 4, lines 22-26 (probes), the sentence bridging pages 5 and 6 (helper oligonucleotides), and page 31, lines 7-9 (amplification oligonucleotides). And by "fully hybridizes" is meant that

hybridization of the target binding region to the target nucleic acid is limited to the region of the target nucleic acid defined by the recited target sequence. Thus, Applicants submit that the target binding portions of the claimed probes and oligonucleotides are fully described, by sequence, in the specification and, as such, unequivocally evidence that Applicants were in possession of the claimed invention at the time the application was filed. Accordingly, withdrawal of this rejection is respectfully requested

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 11-23, 29, 37-40, 50-53, 59, 60, 84, 93-99, 106, 107, 114-126, 133-144 and 151-159 stand rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants submit that this rejection is rendered moot by the amendments to the claims. Accordingly, withdrawal of this rejection is respectfully requested.

Applicants submit that the subject application is in condition for allowance and early Notice to that effect is earnestly solicited.

Please charge any fees due in connection with this Reply, including the fee for a three-month extension of time, to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

Certificate of Transmission

I hereby certify that this correspondence (and any referred to as attached) is being sent by facsimile to 703-872-9306 on the date indicated below to Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Respectfully Submitted,

Date: January 5, 2005

By: _____

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